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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/574,819	05/19/2000	Frank P. Luyten	NIH0099.001C1	1648

7590

06/27/2003

Knobbe Martens Olson & Bear LLP  
620 New port Center Drive Sixteenth Floor  
Newport Beach, CA 92660-8016

EXAMINER

ROMEO, DAVID S

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 06/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/574,819

Applicant(s)

LUYTEN ET AL.

Examiner

David S Romeo

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 27-40 is/are pending in the application.
- 4a) Of the above claim(s) 33-40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 27-32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

Art Unit: 1647

### DETAILED ACTION

The request filed on April 18, 2003 (Paper No. 14) for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09574819 is acceptable and a CPA has been established. An action on the CPA follows.

The amendment filed April 18, 2003 (Paper No. 13) has been entered. Claims 27-40 are pending. Claims 33-40 are withdrawn from consideration as being directed to a non-elected invention. See the Office action mailed January 2, 2003 (Paper No. 11) at pages 2-3. Claims 27-32 are being examined.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 27 is rejected under 35 U.S.C. 102(a) as being anticipated by Storm (38, cited by Applicants). Storm discloses mouse genomic DNA encoding GDF-6 (Figure 1 legend, "METHODS"). GDF6 comprises the amino acid sequence of SEQ ID NO: 24, as indicated below:

S43295  
bone morphogenetic protein homolog GDF6 precursor - mouse (fragment)  
N;Alternate names: growth and differentiation factor 6  
C;Species: Mus musculus (house mouse)  
C;Date: 20-Oct-1994 #sequence\_revision 07-Feb-1997 #text\_change 26-May-2000  
C;Accession: S43295  
R;Storm, E.E.; Huynh, T.V.; Copeland, N.G.; Jenkins, N.A.; Kingsley, D.M.; Lee, S.J.  
Nature 368, 639-643, 1994 (April)  
A;Title: Limb alterations in brachypodism mice due to mutations in a new member of the TGF-beta-superfamily.  
A;Reference number: S43294; MUID:94195427; PMID:8145850  
A;Accession: S43295  
A;Molecule type: DNA  
A;Residues: 1-125 <STO>

Art Unit: 1647

A;Cross-references: EMBL:U08338; NID:g488463; PIDN:AAA18779.1; PID:g488464  
 C;Genetics:  
 A;Gene: Gdf6  
 C;Superfamily: inhibin  
 F;1-5/Domain: polybasic protease recognition site #status predicted <PPR>  
 F;6-125/Product: bone morphogenetic protein homolog GDF6 (fragment) #status predicted <MAT>

Query Match 100.0%; Score 182; DB 2; Length 125;  
 Best Local Similarity 100.0%; Pred. No. 6e-18;  
 Matches 31; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 WIITAPLEYEAYHCEGVCDFFPLRSHLEPTNHA 31  
 |||||  
 Db 41 WIITAPLEYEAYHCEGVCDFFPLRSHLEPTNHA 71.

Accordingly, Storm teaches an isolated nucleic acid molecule which codes for a protein of the TGF- $\beta$  family, wherein said protein comprises the amino acid sequence of SEQ ID NO: 24. Furthermore, a chemical composition and its properties are inseparable. Therefore, the properties applicant discloses and/or claims, i.e. "has chondrogenic activity in vivo", are necessarily present in GDF-6.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Storm (38, cited by Applicants) and Neidhardt (9, cited by Applicants).

Storm discloses mouse genomic DNA encoding GDF-6 (Figure 1 legend, "METHODS"). GDF6 comprises the amino acid sequence of SEQ ID NO: 24, as indicated below:

S43295  
 bone morphogenetic protein homolog GDF6 precursor - mouse (fragment)  
 N;Alternate names: growth and differentiation factor 6  
 C;Species: Mus musculus (house mouse)  
 C;Date: 20-Oct-1994 #sequence\_revision 07-Feb-1997 #text\_change 26-May-2000  
 C;Accession: S43295  
 R;Storm, E.E.; Huynh, T.V.; Copeland, N.G.; Jenkins, N.A.; Kingsley, D.M.; Lee, S.J.  
 Nature 368, 639-643, 1994 (April)  
 A;Title: Limb alterations in brachypodism mice due to mutations in a new member of the TGF-beta-superfamily.  
 A;Reference number: S43294; MUID:94195427; PMID:8145850  
 A;Accession: S43295  
 A;Molecule type: DNA  
 A;Residues: 1-125 <STO>  
 A;Cross-references: EMBL:U08338; NID:g488463; PIDN:AAA18779.1; PID:g488464

Art Unit: 1647

.C;Genetics:  
 A;Gene: Gdf6  
 C;Superfamily: inhibin  
 F;1-5/Domain: polybasic protease recognition site #status predicted <PPR>  
 F;6-125/Product: bone morphogenetic protein homolog GDF6 (fragment) #status predicted <MAT>

Query Match 100.0%; Score 182; DB 2; Length 125;  
 Best Local Similarity 100.0%; Pred. No. 6e-18;  
 Matches 31; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 WIIAPLEYEAYHCEGVCDPFLRSHLEPTNHA 31  
 |||||  
 Db 41 WIIAPLEYEAYHCEGVCDPFLRSHLEPTNHA 71.

Accordingly, Storm teaches an isolated nucleic acid molecule which codes for a protein of the TGF- $\beta$  family, wherein said protein comprises the amino acid sequence of SEQ ID NO: 24. Furthermore, a chemical composition and its properties are inseparable. Therefore, the properties applicant discloses and/or claims, i.e. "has chondrogenic activity in vivo", are necessarily present in GDF-6.

Storm also discloses a GDF-5 cDNA clone and that GDF5, GDF6, and GDF7 define a new subgroup of BMP-related factors (page 639, right column, full paragraph 1; Figure 1a; and, Figure 1 legend, "METHODS"). More detailed studies will be required to determine whether related family members can compensate for GDF5 deficiencies in soft tissues (page 642, paragraph bridging left and right columns). Storm does not teach an expression vector comprising an isolated nucleic acid molecule encoding GDF6, a host cell comprising the vector, or a process for the production of GDF-6.

Neidhardt teaches an expression vector comprising a DNA sequence encoding a BMP-related factor designated MP52 (GDF5), a host cell comprising the vector, wherein the host cell is a mammalian host cell, and a process for the production of MP52 comprising culturing the host cell in a culture medium and isolating the MP52 therefrom (paragraph bridging pages 6-7, through paragraph bridging pages 7-8). Neidhardt does not teach an isolated nucleic acid molecule encoding GDF6.

Art Unit: 1647

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make an isolated nucleic acid molecule encoding GDF6, as taught by Storm, and to recombinantly produce the GDF6 using vectors, host cells, and processes, as taught by Neidhardt, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to recombinantly produce the GDF6 in order to perform more detailed studies in order to determine whether related family members can compensate for GDF5 deficiencies in soft tissues or for use in applications using cell culture techniques requiring growth factors for their performance.

The invention is prima facie obvious over the prior art.

### *Conclusion*

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

BEFORE FINAL (703) 872-9306

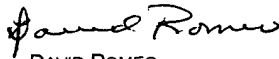
AFTER FINAL (703) 872-9307

IN ADDITION TO THE OFFICIAL RIGHTFAX NUMBERS ABOVE, THE TC 1600 FAX CENTER HAS THE FOLLOWING OFFICIAL FAX NUMBERS: (703) 305-3592, (703) 308-4242 AND (703) 305-3014.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.



DAVID ROMEO  
PRIMARY EXAMINER  
ART UNIT 1647